



# Sleep disturbances and pain among individuals with prescription opioid dependence



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## HIGHLIGHTS

- We examined sleep functioning in prescription opioid (PO) dependent individuals and controls.
- Subjective sleep quality was reportedly less for the PO group than controls.
- As measured by actigraphy, objective sleep quality was less for PO group on 4 of 6 measures.
- This significant sleep impairment indicates the need for close assessment and treatment.

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## ABSTRACT

**Background:** Poor sleep quality has been observed in individuals with substance use disorders and is often a trigger for relapse. To date, little research has investigated sleep quality among individuals with prescription opioid (PO) dependence. The present study aimed to address this gap in the literature by examining subjective and objective sleep disturbances among PO dependent individuals.

**Methods:** Subjects were 68 non-treatment seeking individuals (33 PO dependent, 35 healthy controls). Subjective sleep was assessed with the Pittsburgh Sleep Quality Index (PSQI) and Insomnia Severity Index (ISI). Subjects were admitted for an overnight inpatient hospital stay during which objective sleep data was collected using an actigraphy device. Self-report pain was measured with the Brief Pain Inventory.

**Results:** Significant group differences in subjective sleep quality were revealed in the PSQI ( $p < 0.01$ ) and ISI ( $p < 0.01$ ). Poor sleep quality (i.e., PSQI total score  $> 5$ ) was identified in 80.6% of the PO group, as compared to 8.8% of the control group ( $p < .001$ ). Significant group differences in sleep quality were identified in five of six actigraphy variables: total time asleep, sleep efficiency, latency of onset of sleep, total time awake and time mobile. Furthermore, significant associations between pain severity and sleep quality were observed. **Conclusions:** Results indicate high rates of sleep impairment and poor sleep quality among PO dependent individuals. Pain severity was significantly correlated with sleep quality. Although preliminary, the findings highlight the importance of assessing and treating sleep disturbances, as well as pain, among patients with PO dependence.

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## 1. Introduction

The non-medical use of prescription opioids (PO) is a growing problem in the United States. Data from the National Survey on Drug Use and Health (NSDUH;  $N = 55,279$ ) showed that 13.6% of respondents endorsed lifetime non-medical PO use and 5.1% endorsed non-medical use in the previous year (Back, Payne, Simpson, & Brady, 2010). Similarly, McCabe, Teter, Boyd, Knight, and Wechsler (2005) found a lifetime prevalence of 12% and past year prevalence of 7% in a nationally representative sample of college students ( $N = 10,904$ ). Impairment in

functioning across a variety of domains (e.g., medical, legal, occupational) is often evident among individuals with PO dependence (Miller, 2004). Additionally, the incidence of emergency room visits, overdoses and unintentional fatalities from non-medical PO misuse have increased significantly over the past two decades (Paulozzi, Budnitz, & Xi, 2006; Strassels, 2009).

Motives for non-medical PO use vary and a significant proportion of individuals report initiating PO use for pain management, but then subsequently using the medication for alternative reasons (Back, Lawson, Singleton, & Brady, 2011), such as to improve sleep (Rigg & Ibanez, 2010). Boyd, McCabe, Cranford, and Young (2006) showed in a sample of adolescents ( $N = 1086$ ) that 12% had engaged in non-medical PO use in the previous year and that of those, over 10% were using POs to aid sleep. Among a sample of adult lifetime non-medical PO users ( $N =$

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640) McCabe, Cranford, Boyd, and Teter (2007) found that 13.7% used POs to improve sleep.

Poor sleep quality has been observed in individuals with substance use disorders including alcohol (Brower, 2001), nicotine (Jaehne, Loessl, Bárkai, Riemann, & Hornyak, 2009), marijuana (Bolla et al., 2008), and heroin (Hsu et al., 2012) and often serves as a salient trigger for relapse such that substance users reporting poor sleep are at greater risk for relapse and sleep disturbance is predictive of treatment outcome (Bower & Perron, 2010; Wang & Teichtahl, 2007). Sleep problems can persist for weeks and months, and sometimes years, after substance use cessation (Brower, 2003; Peles, Schreiber, Hamburger, & Adelson, 2011). One study of 60 alcohol-dependent patients found that poor sleep, specifically sleep latency, was the best predictor of relapse after a 12-week inpatient program (Foster & Peters, 1999). In another study by Brower, Aldrich, Robinson, Zucker, and Greden (2001), 60% of alcohol-dependent patients with baseline insomnia had relapsed at 5-months post treatment, as compared to 30% of patients without baseline insomnia. Additionally, significantly higher rates of relapse were observed among patients who endorsed, as compared to those who did not endorse, using alcohol to self-medicate symptoms of insomnia (59.5% vs. 37.8%; Brower et al., 2001).

To date, the research investigating sleep among opioid users has focused on heroin users, primarily in methadone maintenance treatment (MMT) (Sharkey et al., 2011). Stein et al. (2004) reported that 83.9% of 225 MMT patients had Pittsburgh Sleep Quality Index (PSQI) scores indicating poor sleep quality (i.e.,  $>5$ ). In a study of opioid naïve individuals, sleep architecture was significantly altered after a single opioid medication administration, with participants evidencing increases in the percentage of time spent in light sleep stages, and a marked reduction in the percentage of time spent in deep sleep stages (Dimsdale, Norman, DeJardin, & Wallace, 2007). Multiple mechanisms of action leading to disturbed sleep in those abusing opioids have been theorized, including decreased REM sleep (Lydic & Baghdoyan, 2005), altered GABA functioning (Watson, Lydic, & Baghdoyan, 2007), and lowered levels of adenosine (Trksak et al., 2010). Though sleep has become a focus of substance use research, no known studies to date have utilized actigraphy with a group of current PO dependent individuals. An actigraphy device, usually a watch, collects data about body movement continuously while it is worn thus allowing computer programs to determine sleep–wake cycles (Martin & Hakim, 2011).

The present study aimed to expand the extant literature on the presence and characteristics of sleep impairment among individuals with PO dependence. Specifically, we examined subjective self-report measures as well as actigraphy data collected during an overnight hospital stay. We hypothesized that PO dependent individuals, in comparison to healthy controls, would demonstrate poorer sleep quality, as measured by subjective and objective assessments. In addition, associations between poor sleep quality and pain severity were assessed.

## 2. Methods

### 2.1. Participants

Participants ( $N = 68$ ) were 33 non-treatment seeking individuals with current (i.e., past 6 months) PO dependence and 35 healthy controls participating in a larger study on stress, the hypothalamic–pituitary–adrenal (HPA) axis, and prescription opioids. Participants were recruited primarily through advertisements (e.g., newspapers, Craigslist) and were initially screened over the telephone for study eligibility. A total of 220 participants were invited to the in person baseline assessment. Of these, 70 continued in the study, 79 were deemed ineligible, and 71 dropped out.

Exclusion criteria for all participants included the following: pregnant or nursing; major medical or psychiatric conditions that could interfere with the HPA axis (e.g. depression, PTSD, significant hematological, endocrine, cardiovascular, pulmonary, renal, or neurological disease,

including diabetes); use of antihypertensive medications, beta-blockers, synthetic glucocorticoid therapy, or treatment with other agents in the past month that may interfere with the HPA axis response; BMI  $\geq 39$ ; and younger than 18 years old. Exclusion criteria specific to the PO group included the use of methadone in the past three months and meeting DSM-IV criteria for current substance dependence on other substances. Individuals who met criteria for abuse on other substances had to identify PO as their primary drug of choice. Exclusion criteria specific to the control group included current or lifetime substance dependence (other than nicotine) and abuse (other than past alcohol abuse). No participants were taking sleep medications during the time of the study.

### 2.2. Procedure

Participants were informed about all study procedures and IRB-approved written informed consent was obtained before any study procedures occurred. Following a preliminary telephone screen, participants came into the office and completed a baseline visit to determine eligibility. The baseline visit consisted of a structured clinical interview to assess substance use disorders and comorbid psychiatric conditions, self-report measures assessing constructs related to opioid dependence including sleep, a urine drug screen and breathalyzer test, and a history and physical examination. Eligible participants (both PO and healthy controls) were scheduled for a one-night hospital stay at the Medical University of South Carolina (MUSC).

Prior to admission for the overnight stay, three days of abstinence from alcohol and other substances, including PO, as evidenced by self-report, breathalyzer, and urine drug screen, were required. Caffeine and nicotine during the three days prior to the overnight stay were allowed. Participants were admitted to the MUSC hospital at 2000 h the evening prior to testing to allow for the control of extraneous variables (e.g., sleep, caffeine intake) that could potentially affect stress reactivity. Opiate withdrawal symptoms were assessed at the time of hospital admission using the 10-item self-report Short Opiate Withdrawal Scale (SOWS; Gossop, 1990). Participants with a SOWS score indicating acute withdrawal were rescheduled. Cigarette smokers were provided with a nicotine patch upon admission. Twenty-four hour nicotine replacement therapy was maintained throughout the hospital stay ( $\geq 20$  cigarettes/day = 21 mg patch; 10–19 cigarettes/day = 14 mg patch; 5–9 cigarettes/day = 7 mg patch). Participants were provided a standard breakfast at 0730 h and then escorted by research staff to laboratory for testing. The current study does not include data from the laboratory testing. Participants were compensated \$50 for completing the assessment battery and \$150 for completing the hospital overnight.

### 2.3. Measures

#### 2.3.1. Demographic information

Relevant demographic information (e.g., age, gender, employment status) was assessed with a form created for the purposes of this study.

#### 2.3.2. Substance use

Substance use disorders were assessed with the Structured Clinical Interview for DSM-IV (SCID; First, Spitzer, Gibbon, & Williams, 2002). The Timeline Follow-Back (TLFB; Sobell & Sobell, 1992) was used to assess substance use (e.g., PO, heroin, alcohol, marijuana, and cocaine) in the one month prior to the baseline visit. For each substance assessed, two summary variables were generated: 1) percent days used during the past month, and 2) average amount of substance used per day. The Addiction Severity Index, Lite (ASI – Lite; McLellan, Cacciola, & Zanis, 1997) assessed areas of functioning impacted by substance use disorders: 1) medical status, 2) employment status, 3) alcohol use, 4) drug use, 5) legal status, 6) family/social status, and 7) psychiatric status. A recent review of subscale scores by Cacciola, Alterman, Habing,

and McLellan (2011) demonstrated that internal validity scores for the seven subscales ranged from 0.71 (Family/Social problems) to 0.94 (Drugs). On Track Test Cup® (Roche Diagnostics) multi-panel urine drug screen (UDS) test was used to screen for opiates, oxycodone, THC (Marijuana), cocaine, methamphetamines, methadone, and amphetamines.

### 2.3.3. Sleep

During the overnight hospital stay, subjects wore a Respironics® Actiwatch, which is a small, wristwatch-sized device that collects and stores data at regular intervals during the night (e.g., number of hours in bed, number of times out of bed). The following six summary variables can be calculated using Respironics software: sleep latency (time to fall asleep), total time asleep, sleep efficiency (defined as the ratio of time spent in bed to total time asleep), time mobile, total time awake and number of wake bouts. Actigraphy has been shown to be a valid sleep assessment method for insomnia and other sleep problems (Ancoli-Israel et al., 2003; Vallières & Morin, 2003).

Participants completed psychometrically sound self-report forms assessing sleep, including the Pittsburgh Sleep Quality Index (PSQI; Buysse, Reynolds, Monk, Berman, & Kupfer, 1989) and the Insomnia Severity Index (ISI; Morin, Belleville, Bélanger, & Ivers, 2011). The PSQI is an instrument that measures sleep quality in seven domains over the past month: 1) subjective sleep quality, 2) latency, 3) sleep duration, 4) habitual sleep efficiency, 5) sleep disturbances, 6) sleep medication and 7) daytime dysfunction. Participants rate each domain on a 0–3 Likert scale, with higher scores indicating greater levels of sleep disturbance. The domain ratings are summed to produce a total score. A total score greater than 5 is indicative of poor sleep quality. The ISI contains 7 items that are rated on a 0–4 Likert scale. The items are summed to produce a total sleep quality rating, with higher scores indicating poorer sleep quality. Total scores of 0–7 indicate no clinically significant insomnia, 8–14 indicate sub-threshold insomnia, 15–21 indicate moderate clinical insomnia, and 22–28 indicate severe clinical insomnia. Cronbach's alpha for the PSQI and ISI were .82 and .94, respectively.

### 2.3.4. Pain

The Brief Pain Inventory (BPI; Cleeland & Ryan, 1994) is a 17-item self-report measure used to assess the intensity of pain and the degree to which pain interferes with functioning. Two subscales are generated from the BPI: 1) the pain severity scale, which consists of four items that assess the worst and least amount of pain experienced in the past 24 h, average pain, and current pain; and 2) the pain interference scale, which consists of nine items that assess whether and how much pain has interfered with functioning (e.g., mood, sleep, ability to walk). The BPI also includes items assessing the location of the pain, and the amount and duration of relief derived from pain treatments. A high degree of internal consistency (Cronbach's alpha) was evidenced in both the pain severity scale (.94), and pain interference scale (.96).

### 2.4. Statistical analyses

Descriptive statistics and measures of central tendency (e.g., means, standard deviations, and frequencies) were used to summarize the demographic characteristics, sleep variables and other assessments. Independent samples t-tests and Pearson's chi-square tests were used to test differences between the PO and the control group for the PSQI, ISI, and BPI measures. To examine study hypotheses regarding objective sleep quality, a series of ANCOVA analyses were conducted using PROC GLM in SAS Statistical Software. The primary dependent measures were actigraphy outcomes. All models were initially controlled for depression severity, BPI severity, and SOWS scores, however, no covariates were retained in the final model as none controlled for a significant amount of variance in any models. Pearson's correlation coefficient was used to measure linear relationships between variables. Given the preliminary nature of this study,  $\alpha = .05$  for all analyses.

## 3. Results

### 3.1. Demographics

The average age was  $34.5 \pm 12.0$  years (PO group =  $36.0 \pm 12.5$  vs. control group =  $33.2 \pm 11.5$ ). No significant group differences were observed with regard to age, gender or race. Significant group differences in education, employment, marital and smoking status were revealed (see Table 1).

### 3.2. Substance use

As can be seen in Table 1, significant group differences were revealed in the majority of the ASI subscales. Specifically, the PO group evidenced greater impairment in the employment, drugs, legal, family/social and psychiatric subscales, as compared to the control group.

The PO group reported an average of  $12.6 \pm 9.2$  years of PO use, with the age of first use at 23.5 years old. PO dependent subjects reported using PO on 64.1% of days in the month prior to baseline screening visit, with an average of  $3.0 \pm 2.8$  pills consumed per day. The average number of days since last opioid use before hospital admission was  $6.0 \pm 3.6$  days. The PO group evidenced some history of alcohol, cocaine, and marijuana use disorders (see Table 2). The PO group reported low SOWS score at the time of hospital admission ( $8.59 \pm 7.46$ ).

### 3.3. Sleep

Table 3 includes the self-report indices of sleep. Among the PO group, 80.6% reported poor sleep quality (as defined as  $>5$  on the PSQI), compared to 8.8% of the control group ( $p < .001$ ). Mean PSQI total scores for the PO and control groups were  $8.58 \pm 3.77$  and  $2.79 \pm 1.59$ , respectively ( $p < .001$ ). As shown in Fig. 1, PO dependent subjects scored a mean ISI total of  $10.21 \pm 7.64$ , compared to the control mean of  $2.91 \pm 3.74$  ( $p < .001$ ). Sub-threshold insomnia was reported in 41.9% of the PO dependent group, compared to 8.8% of the control group ( $p < .01$ ). Furthermore, 19.4% of PO dependent subjects reported moderate or severe clinical insomnia. The ISI total score for the total sample correlated positively with the PSQI total score ( $r = .83, p < .001$ ).

**Table 1**  
Demographic and clinical variables of prescription opioid (PO) dependent, control, and combined (total) groups.

Demographic characteristics				
Variable	Total	PO dependent	Control	p Value
N (%)	N = 68	n = 33	n = 35	
Male	34 (50)	16 (48.5)	18 (51.4)	0.81
Caucasian	54 (79.4)	26 (78.8)	28 (80)	0.55
African American	6 (8.8)	2 (6.1)	4 (11.4)	
Hispanic	3 (4.4)	2 (6.1)	1 (2.9)	
Other	5 (7.4)	3 (9.1)	2 (5.8)	
Some college or more	56 (82.4)	22 (66.7)	34 (97.1)	0.001
Unemployed	24 (35.3)	21 (63.6)	3 (8.6)	<.001
Not married	50 (73.5)	29 (87.9)	21 (60)	0.03
Smoke	33 (48.5)	29 (87.9)	4 (11.4)	<.001
Current Axis I diagnosis	20 (29.4)	17 (51.5)	3 (8.6)	<.001
Mean $\pm$ Std				
Addiction Severity Index				
Medical	0.10 $\pm$ .23	0.15 $\pm$ .29	0.06 $\pm$ .13	.084
Employment	0.30 $\pm$ .33	0.44 $\pm$ .41	0.17 $\pm$ .12	<.001
Alcohol	0.07 $\pm$ .08	0.07 $\pm$ .09	0.07 $\pm$ .68	.952
Drugs	0.11 $\pm$ .13	0.22 $\pm$ .11	0.00 $\pm$ .00	<.001
Legal	0.05 $\pm$ .12	0.10 $\pm$ .17	0.00 $\pm$ .00	.001
Family/social	0.08 $\pm$ .12	0.13 $\pm$ .15	0.04 $\pm$ .08	.003
Psychiatric	0.09 $\pm$ .15	0.16 $\pm$ .19	0.02 $\pm$ .04	<.001
BPI pain severity	1.68 $\pm$ 2.21	3.16 $\pm$ 2.37	0.32 $\pm$ .64	<.001
BPI pain interference	1.28 $\pm$ 2.09	2.58 $\pm$ 2.43	0.09 $\pm$ .27	<.001

Note: BPI = Brief Pain Inventory.

**Table 2**

Demographic and clinical variables of prescription opioid (PO) dependent, control, and combined (total) groups.

Demographic characteristics				
Variable	Total	PO dependent	Control	p Value
N (%)	N = 68	n = 33	n = 35	
History alcohol dependence	13 (19.1)	13 (39.4)	0	<.001
History alcohol abuse	13 (19.1)	7 (21.2)	6 (17.1)	.675
History marijuana dependence	9 (13.2)	9 (27.3)	0	.002
History marijuana abuse	5 (7.4)	5 (15.2)	1 (2.9)	.018
History cocaine dependence	12 (17.6)	12 (36.4)	0	<.001
History cocaine abuse	1 (1.5)	1 (3.0)	0	.307
History sedative dependence	1 (1.5)	1 (3.0)	0	.307
History sedative abuse	1 (1.5)	1 (3.0)	0	.307

Objective sleep measurements were obtained using an actigraphy device, and the findings revealed significant group differences in five of six sleep variables measured. As shown in Table 3, PO dependent subjects, in comparison to controls, evidenced significantly lower total time asleep, sleep efficiency, greater latency of onset of sleep, total time awake, and time mobile ( $p < .05$ ).

Correlations between subjective and objective sleep measures were examined. No significant correlations between subjective sleep scores and actigraphy data were observed for PO subjects ( $r$  range .04 to .32), controls ( $r$  range .04 to .25) or combined groups ( $r$  range .03 to .24).

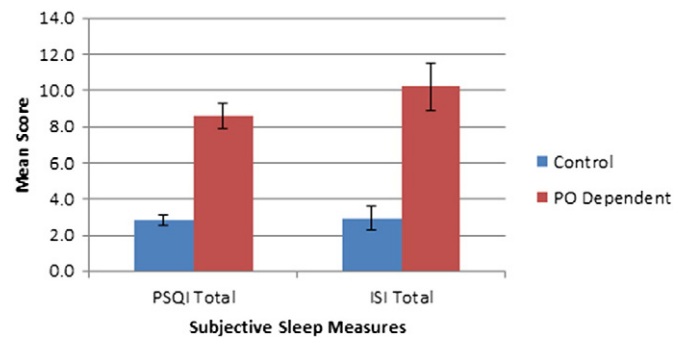
### 3.4. Pain

Pain severity and pain interference, as assessed using the BPI, were significantly higher in the PO group as compared to the control group ( $p < .001$ ; see Table 1). Examination of the relationship between subjective sleep and pain revealed significant correlations. The PSQI total score correlated positively with average pain severity ( $r = .56$ ,  $p < .01$ ) and pain interference ( $r = .40$ ,  $p < .01$ ) for the PO group. Similarly, the ISI total score correlated positively with average pain severity ( $r = .47$ ,  $p < .01$ ) and pain interference ( $r = .46$ ,  $p < .001$ ) for the PO group. No significant correlations observed for the control group for ISI total score and pain severity ( $r = .15$ ,  $p > .05$ ) or pain interference ( $r = .27$ ,  $p > .05$ ). No significant correlations were revealed between actigraphy data and pain for either the PO group (range .05 to .20,  $p > .05$ ) or the control group (range .005 to .28,  $p > .05$ ).

## 4. Discussion

The association between substance use disorders and poor sleep quality has been well documented, with poor sleep serving as a trigger

## Subjective Sleep Group Differences



**Fig. 1.** PSQI and ISI subjective sleep measures among PO dependent individuals and controls.

for relapse. Despite the remarkable rise in the prevalence and deleterious health consequences associated with PO use disorders over the past two decades, little research has examined sleep disturbances among PO dependent individuals. To our knowledge, the current study is the first to report on sleep quality among PO dependent individuals using both objective (actigraphy) and subjective self-report measures. Similar to prior research examining individuals with heroin dependence (Assad, Ghanem, Abdel Samee, & El-Habiby, 2011; Sharkey et al., 2011), the current study found significantly poorer objective and subjective quality of sleep among PO dependent individuals in comparison to healthy controls.

Actigraphy data indicated poorer outcomes among PO dependent individuals on five of six sleep indices, including: 1) less total time asleep, 2) longer latency to sleep onset, 3) more total time awake, 4) more time mobile during the night, and 5) sleep efficiency. Similarly, PO dependent individuals exhibited self-reported sleep disturbance (assessed by the PSQI) and sub-threshold insomnia (assessed by the ISI) that were approximately 10 and 4.5 times higher, respectively, than controls. In accordance with these findings, prior research has documented deficits in sleep functioning among other opioid dependent populations, including individuals entering methadone maintenance treatment (Dyer & White, 1997; Puigdollers et al., 2004; Sharkey et al., 2011; Wang et al., 2005), treatment seeking heroin dependent individuals (Burke et al., 2008), and recipients of long-term opioid agonist therapy (Peles, Schreiber, & Adelson, 2006; Stein et al., 2004). The importance of continued investigation of the effects of PO dependence on sleep are underscored by data suggesting that the effects of opioids on sleep may be greater than that of other substances of abuse (Casola, Goldsmith, Daiter, & Varenbut, 2006), and that sleep

**Table 3**

Subjective sleep and actigraphy measurements for prescription opioid (PO) dependent, control, and combined (total) groups.

Subjective sleep measurements	Total	PO dependent	Control	p Value
Mean ± Std	N = 68	n = 33	n = 35	
PSQI total	5.55 ± 4.10	8.58 ± 3.77	2.79 ± 1.59	<.001
ISI total	6.51 ± 7.0	10.21 ± 7.64	2.91 ± 3.74	<.001
N (%)				
Poor sleep quality (PSQI > 5)	28 (43.1)	25 (80.6)	3 (8.8)	<.001
Subthreshold insomnia (ISI 8–14)	16 (24.6)	13 (41.9)	3 (8.8)	0.014
Moderate or severe clinical insomnia (ISI > 14)	7 (10.8)	6 (19.4)	1 (2.9)	0.001
Actigraphy sleep measurements				
Mean ± Std				
Time to fall asleep (min)	39.64 ± 46.90	52.09 ± 56.43	27.92 ± 32.40	0.035
Sleep efficiency	77.84 ± 12.59	74.69 ± 11.97	80.80 ± 12.62	0.048
Total time asleep (min)	377.70 ± 54.88	360.11 ± 59.11	394.26 ± 45.45	0.010
# of wake bouts	38.12 ± 16.33	40.41 ± 14.30	35.97 ± 17.98	0.27
Total time awake (min)	38.30 ± 26.27	45.72 ± 27.21	31.30 ± 23.67	0.025
Time mobile (min)	33.20 ± 22.45	39.57 ± 24.55	27.21 ± 18.73	0.024

Note. PSQI = Pittsburgh Sleep Quality Index, ISI = Insomnia Severity Index.



architecture is negatively affected during each stage of opioid dependence: induction, maintenance, acute abstinence, and protracted abstinence (for review see Wang & Teichtahl, 2007).

Chronic pain is common among individuals with PO dependence and may help explain the association between PO dependence and poor sleep quality. In comparison to controls, PO dependent participants in the current study reported experiencing greater pain severity and pain interference, and their pain was significantly correlated with the PSQI and ISI subjective measures of sleep quality. These findings are consistent with literature demonstrating significant interrelations between chronic pain conditions, sleep disruption, and PO dependence (Onen, Onen, Courpron, & Dubray, 2005). Of note, a substantial proportion of opioid dependent individuals report regulation of sleep as a significant motivator for use (Burke et al., 2008; McCabe, Boyd, Cranford, & Teter, 2009; Rigg & Ibanez, 2010). Conversely, neurobiological research indicates that use of exogenous opioids that block endogenous opioid peptide receptors are also active in the regulation of sleep, thereby impacting sleep architecture and contributing to increased latency of sleep onset, decreased REM sleep, increased waking bouts, and greater sleep fragmentation (Aghajanian, 1978; Dimsdale et al., 2007; Lord, Waterfield, Hughes, & Kosterlitz, 1977; Wang & Teichtahl, 2007). Research examining the unique contributions of pain versus opioid use on sleep quality is limited. Shaw, Lavigne, Mayer, and Choiniere (2005) found that acute administration of opioids to healthy, pain-free, non-dependent adults resulted in significant disruption of sleep architecture, suggesting that opioid use accounts for significant variance in sleep quality even in the absence of chronic pain. Further, both opioid use and increased pain intensity have been implicated in exacerbation of central sleep apneic events, although opioid use contributed significantly more variance to the frequency of apneic events than pain intensity (Jungquist, Flannery, Perlis, & Grace, 2012).

Although the current findings document a consistent association between PO dependence and poorer sleep assessed via both objective and subjective methods, subjective measures of sleep were not significantly correlated with objective measures of sleep for either the PO or control group subjects. This pattern of results is consistent with a growing literature documenting discrepancies between objective and subjective measures of sleep quality, as well as differential predictors of sleep quality by method of assessment (Silva et al., 2007; Van Den Berg et al., 2008). Of note, both modes of sleep assessment have limitations: actigraphy-based data are best interpreted as a proxy assessment of sleep quality rather than a direct measure of the depth or quality of sleep, and self-report data are subject to recall biases (Krystal & Edinger, 2008). Whereas factors such as depressed mood, elevated stress, poor overall health status, and low social support are stronger predictors of self-reported sleep efficiency, factors such as BMI, employment, sleep apnea, medication use, and sleep/wake times are stronger predictors of actigraphy-based assessments of sleep quality (Dhruva et al., 2012; Jackowska, Dockray, Hendrickx, & Steptoe, 2011; Sharkey et al., 2010; Tworoger, Davis, Vitiello, Lentz, & McTiernan, 2005). Given the unique limitations associated with each method of sleep assessment, obtaining both subjective and objective data has been recommended (Van Den Berg et al., 2008).

This study has several limitations that warrant consideration. A relatively small sample size may limit the generalizability of the findings. The study design also necessitated an overnight stay in the hospital, potentially increasing participants' anxiety. The change of environment and evening routine may have also increased sleep disturbances. The data are cross-sectional in nature and some assessments employed in the study assessed different timeframes (e.g., substance use was assessed over the past 30 days, pain was assessed over the past 24 h). Therefore, the current study cannot address the temporal order of onset of PO dependence and sleep disruption, or the role of poor sleep quality in maintaining PO dependence. The use of both subjective and objective assessments of sleep is a notable strength of the current study; however, objective measurement of sleep consisted of

actigraphy-based data that was limited to a single, in-lab, overnight observation. Although actigraphy is an accepted and commonly used method for sleep assessment and is endorsed for use in community sleep research by the American Academy of Sleep Medicine (Kushida et al., 2001; Lichstein et al., 2006; Morgenthaler et al., 2007; Onen et al., 2005), this methodology has limitations. For example, actigraphy may be less accurate in measuring sleep latency and is prone to first night effects. Future research would benefit from the collection of more in-depth sleep quality data utilizing polysomnographic methods that alleviate first night effects and allow for assessment of sleep apneic events (Krystal & Edinger, 2008; Kurth, Sharkey, Millman, Corso, & Stein, 2009; Sharkey et al., 2011; Stein et al., 2012). Finally, future research may also be informed by the extension of the assessment timeframe and environment (i.e., to naturalistic home environment).

In summary, the results of the current study indicate marked reductions in sleep quality among non-treatment seeking PO dependent individuals, as well as a significant association between pain and sleep disruption. Given the complex roles that poor sleep quality and chronic pain may play in the initiation, maintenance and relapse to substance use (Brower et al., 2001), the current findings highlight the importance of assessing and treating sleep disturbances as well as pain conditions among PO dependent individuals as these may increase risk for relapse as patients attempt to self-medicate with opioids. Much remains to be investigated in future research, including increased understanding of the discrepancy in self-report and objective measures, the role of chronic PO use in sleep disruption, the role of pain in the maintenance of PO use, and the association of pain and sleep disruption in PO users.

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#### Contributors

Dr. Back designed the study and wrote study protocol. Mr. Pfeifer, Dr. McCauley, and Ms. Hartwell conducted literature searches and wrote the first draft of the manuscript. Mr. Pfeifer & Dr. Moran authors conducted statistical analyses. All authors approved the final draft.

#### Conflict of Interest

The authors declare that they have no competing financial interests or conflict of interest relating to the data included in this manuscript. The authors declare that, except for income received from primary employer, no financial support or compensation has been received from any individual or corporate entity relevant to the data in this manuscript. There are no personal financial holdings that could be perceived as constituting a potential conflict of interest for this manuscript.

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